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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,270	09/24/2001	Gerd Geisslinger	016915-0244	2372

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,270	GEISSLINGER ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-32 and 35-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32 and 35-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.00

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted June 13, 2005 is acknowledged.

Claim Rejections 35 U.S.C. § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Geisslinger et al. (US 5,200,198, of record).

Geisslinger et al. (US 5,200,198) teaches a method of treating painful and/or inflammatory diseases and/or with fever with the flurbiprofen in pure or preponderantly R(-)flurbiprofen. The effective amount is about 0.25 to 5 mg/kg of body weight, which may be administered in 2-5 portion within a day. See, particularly, the abstract and column 6, lines 15-24.Geisslinger particularly discloses an oral dosage form of tablets, dragees and gelatin capsule effective in treating diseases characterized by pain or inflammation comprising 75 or 100 mg. of 99.5% percent R-flurbiprofen, pharmaceutical adjuvants and carriers, see col. 7 line 54 to col. 8 line 3, see col. 5, lines 3-10. Geisslinger et al. further teaches the particular salts recited herein, i.e., salts of alkali metals, alkaline earth metals, ammonium and amino acid salts, in particular lysinate, see claims 1-9 in particular. Geisslinger et al. teaches that the medicament comprises retarding additives, see claim 10 for example. Geisslinger finally teaches a dosage form comprising a rapidly and retardedly inflowing form, see claims 10-11.

Claim Rejections 35 U.S.C. § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-32, 36-38, 45-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geisslinger et al. (US 5,200,198, of record) and Brune et al. (US 5,206,029), in view of Berkow et al. (of record).

Geisslinger et al. (US 5,200,198) teaches a method of treating painful and/or inflammatory diseases and/or with fever with the flurbiprofen in pure or preponderantly R(-)flurbiprofen. The effective amount is about 0.25 to 5 mg/kg of body weight. See, particularly, the abstract and column 6, lines 15-24. Brune et al. disclosed that the active agents may be administered in 1-5 portions with a day depending on the particular dosage form. See, particularly, column 6, lines 53-61. Geisslinger et al. particularly discloses an oral dosage form of tablets,

dragees and gelatin capsule effective in treating diseases characterized by pain or inflammation comprising 75 or 100 mg. of 99.5% pure R-flurbiprofen, pharmaceutical adjuvants and carriers, see col. 7 line 54 to col. 8 line 3. Geisslinger et al. further teaches the particular salts recited herein, i.e., salts of alkali metals, alkaline earth metals, ammonium and amino acid salts, in particular lysinate, see claims 1-9 in particular. Geisslinger et al. finally teaches that the medicament comprises retarding additives, see claim 10 for example. Geisslinger et al. also

teaches a medicament comprising from about 95%:5% to about 60%:40% of R-flurbiprofen: S-flurbiprofen. Geisslinger et al. also teaches that each unit dosage form can contain from 10 to 100

mg of the enantiomer mixture, see cols. 7-8 and claim 3 in particular. Geisslinger finally teaches a dosage form comprising a rapidly and retardedly inflowing form, see claims 10-11.

Geisslinger et al. does not particularly teach the diseases herein, or the dosage herein.

However, Berkow et al. teaches that rheumatic diseases, asthma, inflammatory intestinal disease such as colitis and Crohn's disease, arteriosclerosis, and some immune diseases are known to be caused by inflammation and accompanied by pain.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ R-flurbiprofen in treating any disease associated with pain and inflammation.

One of ordinary skill in the art would have been motivated to employ R-flurbiprofen in treating any disease associated with pain and inflammation because the prior art broadly teaches that R-flurbiprofen is useful in treating any disease associated with pain and inflammation and all diseases herein are known to be associated with both pain and inflammation. As to the dosage recited in claims 36-38, note Geisslinger or Brune disclosed the effective amounts of 0.25 to 5 mg/kg of body weight. A single dosage of 300 mg for a person of 60 kg body weight would be within the range disclosed by Brune.

Claims 35, 39-44, and 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geisslinger et al. (US 5,200,198, of record) and Brune et al. (US 5,206,029), in view of

Berkow et al. (of record) for reasons discussed above, in further view of Wechter et al. (US 5,981,592) and Ghio et al. (US 5,840,277).

Geisslinger et al., Brune et al. and Berkow taken together do not teach expressly to use dosage more than 1000 gm, or to identifying human subject suffering from a disease influenced by the inhibition of NF-kappaB production.

However, Wechter et al. teaches that for treating neoplastic disorders (tumors) or cystic fibrosis, a inflammatory disorder, the dosage of R-NSAID, including flurbiprofen, may be up to 2000 mg. See, particularly, column 3-4 and the claims. Ghio et al. discloses that it is known in the art that inflammatory diseases such as cystic fibrosis, asthma, are closely associated with cytokines, which are regulated by NF-kappaB, and the inhibiting the activity of NF-kappaB are useful for treating inflammatory diseases, such as cystic fibrosis. See, particularly, column 2, line 20 to column 4, line 30, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a dosage of more than 1000 mg of R-NSAID for treating inflammatory diseases such as cystic fibrosis, or to first confirm a human subject having inflammatory diseases such as cystic fibrosis before treating the subject with R-NSAID.

A person of ordinary skill in the art would have been motivated to remove to employ a dosage of more than 1000 mg of R-NSAID for treating inflammatory diseases such as cystic fibrosis, or to first confirm a human subject having inflammatory diseases such as cystic fibrosis before treating the subject with R-NSAID because it is known that the effective amounts R-NSAID may be up to 2000 mg, and inflammatory diseases, such as cystic fibrosis, are known to be influenced

by the activity of NF-kappaB. With respect to claim 50, note the optimization of a result effective parameter, e.g., therapeutic period, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

Response to the Arguments

Applicants' amendments and remarks submitted June 13, 2005 have been fully considered, but are found unpersuasive.

With respect to the rejections of claims 21-32 under 35 U.S.C. 102, Applicants assert that Geisslinger fails to teach each and every element as set forth in the claims, but fail to clearly identify which element is not taught by Geisslinger. Geisslinger teaches to use the same compound (R-flurbiprofen), in the same amount (0.25 to 5 mg/kg of body weight) for treating the same population (subjects with pain and/or inflammation). It is noted that the "disease influenced by the inhibition of NF-kB production" would encompass pain and/or inflammation, See, the original claims 33 and pages 9-12 in the specification.

3. Regarding the rejections under 35 U.S.C. 103, it is noted the cited references suggest the same diseases herein recited. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the teaching, suggestion, and motivation are found

both in the cited references and in the knowledge generally available to one of ordinary skill in the art.

As to claims 35 and 39, applicants further argue that the claim is not obvious because Ghio merely describes the role of NF-kB for inflammation, but does not name R-arypropionic acids as inhibitors or NF-kB. Wechter also fails to recognize R-NSAID as NF-kB inhibitors. The examiner respectfully disagrees. Note the claims read on: 1) identifying a subject with disease influenced by inhibition of NF-kB production; and 2) treating the subject with R-arypropionic acid. Ghio teaches that inflammatory diseases are influenced by the inhibition of NF-kB production. Therefore, identifying a subject with inflammatory diseases and treating the subject with R-arypropionic acid would effectively practice the claimed invention. In response to applicant's argument that the cited references do not teach R-arypropionic acids as inhibitors or NF-kB, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). It is noted that the instant claims are directed to effecting a biochemical pathway with an old and well known compounds. The argument that such claims are not directed to the old and well known ultimate utility (treating painful and/or inflammatory diseases, such as Crohn's disease, cystic fibrosis or tumor) for the compounds, e.g., R-flurbiprofen, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to In re Swinehart, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently

possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical intermediates. The ultimate utility for the claimed compounds is old and well known rendering the claimed subject matter either anticipated by the cited prior art, or obvious to the skilled artisan. It would follow therefore that the instant claims are properly rejected under 35 USC 102, or 103.

The formal drawing submitted August 7, 2003 is acceptable by the examiner.

It is noted that claim 35 improperly depends on claim 21 since it claims 1000mg/ dose or higher, and claim 21 require 100-1000 mg/dose. It is suggested to rewrite claim 35 as an independent claim.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

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Art Unit 1617